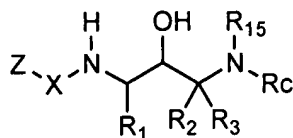


Claim 1. (previously presented) A compound of the formula:



or a pharmaceutically acceptable salt or ester thereof,

wherein Z is aryl, heteroaryl or heterocyclyl, wherein said groups are optionally substituted with 1 or 2 R_B groups, wherein,

where R_B at each occurrence is independently selected from halogen, -OH, -OCF₃, -O-phenyl, -CN, -NR₁₀₀R₁₀₁, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, (CH₂)₀₋₃ (C₃-C₇ cycloalkyl), aryl, heteroaryl, or heterocyclyl wherein, the alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, heteroaryl, or heterocyclyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, halogen, -OH, -CN, or -NR₁₀₀R₁₀₁;

where R₁₀₀ and R₁₀₁ are at each occurrence are independently H, C₁-C₆ alkyl, or phenyl;

X is -(C=O)- or -(SO₂)-;

wherein R₁ is C₁-C₁₀ alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, =O, -SH, -CN, -CF₃, -OCF₃, -C₃₋₇ cycloalkyl, -C₁-C₄ alkoxy, amino, mono-dialkylamino, aryl, heteroaryl, heterocycloalkyl, wherein each aryl group is optionally substituted with 1, 2 or 3 R₅₀ groups;

wherein R_{50} is selected from halogen, OH, SH, CN, $-\text{CO}-(\text{C}_1-\text{C}_4 \text{ alkyl})$, $-\text{NR}_7\text{R}_8$, $-\text{S}(\text{O})_{0-2}-(\text{C}_1-\text{C}_4 \text{ alkyl})$, $\text{C}_1-\text{C}_6 \text{ alkyl}$, $\text{C}_2-\text{C}_6 \text{ alkenyl}$, $\text{C}_2-\text{C}_6 \text{ alkynyl}$, $\text{C}_1-\text{C}_6 \text{ alkoxy}$ and $\text{C}_3-\text{C}_8 \text{ cycloalkyl}$;

wherein the alkyl, alkenyl, alkynyl, alkoxy and cycloalkyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of $\text{C}_1-\text{C}_4 \text{ alkyl}$, halogen, OH, $-\text{NR}_5\text{R}_6$, CN, $\text{C}_1-\text{C}_4 \text{ haloalkoxy}$, NR_7R_8 , and $\text{C}_1-\text{C}_4 \text{ alkoxy}$;

wherein R_5 and R_6 are independently H or $\text{C}_1-\text{C}_6 \text{ alkyl}$; or

wherein R_5 and R_6 and the nitrogen to which they are attached form a 5 or 6 membered heterocycloalkyl ring; and

wherein R_7 and R_8 are independently selected from the group consisting of H; $-\text{C}_1-\text{C}_4 \text{ alkyl}$ optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of $-\text{OH}$, $-\text{NH}_2$, and halogen; $-\text{C}_3-\text{C}_6 \text{ cycloalkyl}$; $-(\text{C}_1-\text{C}_4 \text{ alkyl})-\text{O}-(\text{C}_1-\text{C}_4 \text{ alkyl})$; $-\text{C}_2-\text{C}_4 \text{ alkenyl}$; and $-\text{C}_2-\text{C}_4 \text{ alkynyl}$;

wherein each heteroaryl is optionally substituted with 1 or 2 R_{50} groups;

wherein each heterocycloalkyl group is optionally substituted with 1 or 2 groups that are independently R_{50} or $=\text{O}$;

R₂ and R₃ are independently selected from

-H;

-F;

-C₁-C₆ alkyl optionally substituted with a substituent selected from the group consisting of -F, -OH, -C≡N, -CF₃, C₁-C₃ alkoxy, and -NR₅R₆;

-(CH₂)₀₋₂-R₁₇;

-(CH₂)₀₋₂-R₁₈;

-C₂-C₆ alkenyl or C₂-C₆ alkynyl, wherein each is optionally substituted with an independent substituent selected from the group consisting of -F, -OH, -C≡N, -CF₃ and C₁-C₃ alkoxy;

-(CH₂)₀₋₂-C₃-C₇ cycloalkyl, optionally substituted an independent substituent selected from the group consisting of -F, -OH, -C≡N, -CF₃, C₁-C₃ alkoxy and -NR₅R₆; or

R₂, R₃ and the carbon to which they are attached form a carbocycle of three thru seven carbon atoms, wherein one carbon atom is optionally replaced by a group selected from -O-, -S-, -SO₂-, or -NR₇-;

where R₁₇ at each occurrence is an aryl group selected from phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl and tetralinyl, wherein said aryl groups are optionally substituted with one or two groups that are independently

-C₁-C₃ alkyl; -C₁-C₄ alkoxy; CF₃; or

-C₂-C₆ alkenyl or -C₂-C₆ alkynyl each of which is optionally substituted with one substituent selected from the group consisting of F, OH, C₁-C₃ alkoxy; or

-halogen;

-OH;

-C≡N;

-C₃-C₇ cycloalkyl;

-CO- (C₁-C₄ alkyl);

-SO₂- (C₁-C₄ alkyl);

where R₁₈ is a heteroaryl group selected from pyridinyl, pyrimidinyl, quinolinyl, indolyl, pyridazinyl, pyrazinyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, oxazolyl, thiazolyl, furanyl, thienyl, pyrrolyl, oxadiazolyl or thiadiazolyl, wherein each of said heteroaryl groups is optionally substituted with one or two groups that are independently

-C₁-C₆ alkyl optionally substituted with one substituent selected from the group consisting of OH, C≡N, CF₃, C₁-C₃ alkoxy, and -NR₅R₆;

R₁₅ is selected from the group consisting of hydrogen, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, hydroxy C₁-C₆ alkyl, halo C₁-C₆ alkyl, each of which is unsubstituted or substituted with 1, 2, 3, or 4 groups independently selected from halogen, C₁-C₆ alkyl, hydroxy, C₁-C₆ alkoxy, NH₂, and -R₂₆-R₂₇;

wherein R₂₇ is selected from the group consisting of C₁-C₆ alkyl, C₁-C₆ alkoxy, aryl C₁-C₆ alkyl, heterocycloalkyl, and heteroaryl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C₁-C₄ alkyl, C₁-C₄ alkoxy, halogen, haloalkyl, hydroxyalkyl, -NR₅R₆, -C(O)NR₅R₆;

wherein each R_{245} group is independently selected from the group consisting of

$$-(\text{CH}_2)_{0-4}\text{CO}_2\text{C}_1-\text{C}_4 \quad \text{alkyl}$$

- (CH₂)₀₋₄C(=O)C₁₋₄ alkyl

-C₁-C₄ alkyl,

-C₁-C₄ hydroxyalkyl,

-C₁-C₄ alkoxy,

-C₁-C₄ haloalkoxy,

- (CH₂)₀₋₄-C₃-C₇ cycloalkyl,

- C₂-C₆ alkenyl,
- C₂-C₆ alkynyl,
- (CH₂)₀₋₄ aryl,
- (CH₂)₀₋₄ heteroaryl, and
- (CH₂)₀₋₄ heterocycloalkyl

wherein the aryl, heteroaryl or heterocycloalkyl group included within R₂₄₅ is optionally substituted with 1, 2, or 3 groups that are independently halogen, C₁₋₆ alkyl, CN or OH.

Claim 2. (Currently amended) A compound according to claim 1, wherein:

Z is aryl or heteroaryl, wherein each ring is independently optionally substituted with 1 or 2 groups independently selected from halogen, -OH, -OCF₃, -O-phenyl, -CN, -NR₁₀₀R₁₀₁, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, (CH₂)₀₋₃(C₃-C₇ cycloalkyl), aryl, heteroaryl, or heterocyclyl wherein, the alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, heteroaryl, or heterocyclyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C₁-C₄ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, halogen, -OH, -CN, or -NR₁₀₀R₁₀₁.

Claim 3. (original) A compound according to claim 1, wherein X is -(C=O)-.

Claim 4. (original) A compound according to claim 1, wherein:

R₁ is -C₁-C₆ alkyl-aryl, -C₁-C₆ alkyl-heteroaryl, or -C₁-C₆ alkyl-heterocyclyl, wherein each aryl group at each occurrence is optionally substituted with 1, 2 or 3 R₅₀ groups; wherein R₅₀ is independently selected from halogen, OH, SH, CN, -CO-(C₁-C₄ alkyl), -NR₇R₈, -S(O)₀₋₂-(C₁-C₄ alkyl), C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy, or C₃-C₈ cycloalkyl;

wherein the alkyl, alkenyl, alkynyl, alkoxy, or cycloalkyl groups are optionally substituted with 1 or 2 substituents independently selected from the group consisting of C₁-C₄ alkyl, halogen, OH, -NR₅R₆, CN, C₁-C₄ haloalkoxy, NR₇R₈, and C₁-C₄ alkoxy;

wherein R₅ and R₆ at each occurrence are independently H or C₁-C₆ alkyl; or

wherein R₅ and R₆ and the nitrogen to which they are attached, at each occurrence form a 5 or 6 membered heterocycloalkyl ring; and

wherein R₇ and R₈ are independently selected from the group consisting of H; -C₁-C₄ alkyl optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of -OH, -NH₂, and halogen; -C₃-C₆

cycloalkyl; -(C₁-C₄ alkyl)-O-(C₁-C₄ alkyl); -
C₂-C₄ alkenyl; and -C₂-C₄ alkynyl;

wherein each heteroaryl at each occurrence is optionally substituted with 1 or 2 R₅₀ groups;

wherein each heterocycloalkyl group at each occurrence is optionally substituted with 1 or 2 groups that are independently R₅₀ or =O..

Claim 5. (original) A compound according to claim 1, wherein R₂ and R₃ are hydrogen.

Claim 6. (original) A compound according to claim 1, wherein R₁₅ is hydrogen.

Claim 7. (cancelled)

Claim 8. (Cancelled)

Claim 9. (original) A compound according to claim 8 wherein one of x₁, x₂, or x₃ is SO₂.

Claim 10. (original) A compound according to claim 8 wherein one of x₁, x₂, or x₃ is NH.

Claim 11. (original) A compound according to claim 8 wherein x₁, x₂, and x₃ are each CH₂.

Claim 12. (currently amended) A compound according to claim 1 selected from the group consisting of:

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)pyridine-2-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)pyrazine-2-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1-ethyl-3-methyl-1*H*-pyrazole-5-carboxamide;

3-amino-*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-1,2,4-triazole-5-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-5-methylisoxazole-3-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-6-hydroxypyridine-2-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-imidazole-4-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)nicotinamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)-1*H*-pyrazole-4-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)isonicotinamide;

5-chloro-*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[(1*S*)-7-ethyl-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-2-hydroxypropyl)thiophene-2-carboxamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4*S*)-6-neopentyl-3,4-dihydro-2*H*-chromen-4-yl]amino}propyl)benzamide;

N-[(1*S*,2*R*)-3-{[(4*S*)-6-tert-butoxy-3,4-dihydro-2*H*-chromen-4-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4*S*)-6-neopentyl-1,2,3,4-tetrahydroquinolin-4-yl]amino}propyl)benzamide;

N-[(1*S*,2*R*)-3-{[(4*S*)-6-tert-butoxy-1,2,3,4-tetrahydroquinolin-4-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

N-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1*S*)-7-neopentyl-1,2,3,4-tetrahydronaphthalen-1-

yl]amino}propyl)benzamide;

N-[(1S,2R)-3-{[(1S)-7-tert-butoxy-1,2,3,4-tetrahydronaphthalen-1-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;

~~N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4R)-6-neopentyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}propyl)benzamide;~~

~~N-[(1S,2R)-3-{[(4R)-6-tert-butoxy-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;~~

~~N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-neopentylphenyl)cyclohexyl]amino}propyl)benzamide;~~

~~N-[(1S,2R)-3-{[1-(3-tert-butoxyphenyl)cyclohexyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;~~

~~N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-neopentylphenyl)cyclopropyl]amino}propyl)benzamide;~~

~~N-[(1S,2R)-3-{[1-(3-tert-butoxyphenyl)cyclopropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;~~

~~N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4-neopentyl-1,1'-biphenyl-2-yl)methyl]amino}propyl)benzamide;~~

~~N-[(1S,2R)-3-{[(4-tert-butoxy-1,1'-biphenyl-2-yl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;~~

~~N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{(2-neopentyl-9H-fluoren-9-yl)amino}propyl)benzamide;~~

~~N-[(1S,2R)-3-[(2-tert-butoxy-9H-fluoren-9-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide;~~

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4R)-6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-2-hydroxypropyl)-3,5-dimethylbenzamide; and

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4R)-6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-2-hydroxypropyl)-4-(2-methoxyethyl)benzamide.

Claim 13. (canceled).

Claim 14. (previously presented) A method for the treatment or prevention of Alzheimer's disease comprising administration of a therapeutically effective amount of a compound or salt according to Claim 1, to a patient in need thereof.

Claim 15. (original) A method of treatment as in claim 14, wherein the patient is a human.

Claim 16. (cancelled)

Claim 17. (original) A pharmaceutical composition comprising a compound according to claim 1 in combination with a physiologically acceptable carrier or excipient.